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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,188	06/21/2007	Eugen Kolossov	2590.0040002/EJH/UWJ	7273

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STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.  
1100 NEW YORK AVENUE, N.W.  
WASHINGTON, DC 20005

EXAMINER
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CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
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1632

MAIL DATE	DELIVERY MODE
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05/24/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/594,188	<b>Applicant(s)</b> KOLOSSOV ET AL.	
	<b>Examiner</b> Shin-Lin Chen	<b>Art Unit</b> 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 23 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-13, 17, 19-32 and 45-70 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13, 17, 19-32 and 45-70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2-23-10 has been entered.

Applicant's remark filed 2-23-10 has been entered. Claims 1-13, 17, 19-32 and 45-70 are pending and under consideration.

### ***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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4. Claims 1-13, 17, 19-32 and 45-70 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dang et al., June 26, 2003 (US 2003/0119107 A1, IDS) in view of Yan et al., February 2003 (US 20030027331 A1) and Kehat et al., 2001 (The Journal of Clinical Investigation, Vol. 108, No. 3, p. 407-414, IDS) and is repeated for the reasons set forth in the preceding Official action mailed 11-23-09. Applicant's arguments filed 2-23-10 have been fully considered but they are not persuasive.

Applicant argues that the teachings of Dang represent "the current technologies used to culture pluripotent stem cells" and the single cells are singled out in separate containers" the scLSC is a static and batch-style culture and not agitated. Dang teaches encapsulated liquid suspension culture (ESC) in a reactor and the ES cell suspension was cultured in "unagitated" Petri dish. The method of the instant invention is superior to the other conventional methods of embryoid body formation. The ES cells are less exposed to shear stress than conventional spinner flasks or stirring cultures and the ability of the cells to differentiate in an appropriate manner is not negatively influenced. The art cited by Examiner would not have provided a reasonable expectation of success in obtaining the presently claimed methods. Dang shows that efficient EB generation in liquid culture is only possible either under static conditions or aggregation is controlled by encapsulation. The paragraph [0053] of dang should be interpreted under the background that the liquid suspension ES cell culture is under encapsulation condition. Applicant further argues that the Examiner fails to consider the declaration by Dr. Silke Schwengberg. The Schwengberg declaration shows that the agitation method produced a higher yield of EB/ml and yield of differentiated cells/ES cell seeded but Dang does not teach or suggest that rocking of a single cell suspension culture of pluripotent cells would produce high

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volume and density of EBs (remarks, p. 2-8). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 11-23-09. Although the single cell suspension culture mentioned by Dang is static culture, however, Dang teaches a method for efficient formation of EBs and the culture of EBs in suspension at higher cell densities by controlling cell aggregation. The ES cells are encapsulated to control cell aggregation such that each capsule gives rise to one embryoid body and each capsule contains a predetermined number of ES cells that are permitted to aggregate to form a single EB. The phrase “liquid single cell suspension” in the instant invention appears to mean that the cells are trypsinized, centrifuged, and suspended in culture medium to obtain “liquid single cell suspension”. Trypsinization of cells, centrifuged, and suspending the cells in culture medium in agitated condition to grow the cells was well known in the art. The 96-wells single cell suspension culture and the hang-drop suspension culture do not require that every well or every drop only contains one single ES cell rather it contains a small number of ES cells in each well or hang-drop. The specification of the instant invention fails to specifically define the phrase “liquid single cell suspension culture” and there is no limitation in the claims that the ES cells cannot be encapsulated. Therefore, the stirred encapsulated ES cell suspension culture as taught by Dang can also be considered as a type of liquid single cell suspension culture. In fact, Dang teaches stirred ES cell culture (e.g. [0162], [0163]). Encapsulation of ES cells is used to prevent cell aggregation and to obtain higher number of EBs at higher cell density. Thus, in view of the teachings of Dang and the state of prior art, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to rock a liquid single cell suspension of pluripotent cells and there is reasonable expectation to obtain embryoid bodies and differentiation of ES cells to

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cardiomyocytes as claimed. Further, the claims do NOT recite the superior result to the conventional method as indicated in the remarks and Schwengberg declaration. The claimed invention only requires rocking a container containing a liquid single cell suspension culture of pluripotent cells to obtain EBs and to differentiate into cardiomyocytes. Thus, the claims render obvious to one of ordinary skill in the art at the time of the invention in view of the teachings of Dang, Yan and Kehat.

Applicant argues that the deficiencies of Dang are not cured by the disclosure of yan and kehat. Yan and Kehat do not teach or suggest a method for generating embryoid bodies by rocking a single cell suspension of pluripotent cells. None of the references cited by Examiner teach a method of producing EBs from pluripotent cells by rocking a single cell suspension with a concentration of  $0.5 \times 10^6$  to  $5 \times 10^5$  cells/ml or  $0.1 \times 10^6$  to  $1 \times 10^6$  cells/ml (remarks, p. 9-10). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 11-23-09 and the reasons set forth above.

### ***Conclusion***

No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Shin-Lin Chen, Ph.D.  
/Shin-Lin Chen/  
Primary Examiner, Art Unit 1632